Huge impact of assumptions on indirect effects on the cost-effectiveness of routine infant vaccination with 7-valent conjugate vaccine (Prevnar)
Rozenbaum MH, van Hoek AJ, Hak E, Postma MJ

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of routine infant vaccination, with seven-valent pneumococcal conjugate vaccine (PCV-7), taking into account the key assumptions on the indirect effects of vaccination (herd immunity). The authors concluded that the cost-effectiveness of routine infant PCV-7 vaccination depended on the inclusion of the indirect effects, which were uncertain in Europe. The authors’ conclusions appear to be valid, but further studies are needed to corroborate these findings, given some limitations in the analysis.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
This study examined the cost-effectiveness of routine infant vaccination, with seven-valent pneumococcal conjugate vaccine (PCV-7), taking into account key assumptions on its indirect effects (herd immunity).

Interventions
A strategy of routine infant immunisation with PCV-7, in a three-plus-one dose schedule, was compared against no vaccination.

Location/setting
Netherlands/primary care.

Methods
Analytical approach:
The analysis was based on a published static cohort model (Bos, et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details), in which the epidemiological and resource use data were updated. The time horizon was five years. The authors stated that the analysis was carried out from the perspective of society.

Effectiveness data:
The clinical data were from selected studies that included a recent Dutch study, national databases for the epidemiological inputs, and clinical trials for the vaccine efficacy. The key input was the assessment of the indirect effects for those outside the vaccine-protected cohort (herd protection benefits) and these was from three recent studies conducted in the USA.

Monetary benefit and utility valuations:
The utility values were from two published studies.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years (LYs) were the summary benefit measures and they were discounted at an annual rate of 1.5%.

Cost data:
The economic analysis included both the direct medical costs and the indirect non-medical costs of production lost. The resource use data were from Dutch published studies. The cost of vaccine was based on the Dutch price at the time and
included the administration costs. The costs were in Euros (EUR) and the price year was 2008. They were discounted at an annual rate of 4%.

Analysis of uncertainty:
Not investigated.

Results
Without net-indirect effects (herd protection minus serotype replacement), compared with no vaccination, routine immunisation resulted in a net total cost of EUR 30.6 million and gains of 292 LYs or 422 QALYs. The incremental cost was EUR 104,790 per LY gained or EUR 72,360 per QALY gained.

When the net-indirect effects were considered (equal to those found in the USA), the additional costs were EUR 25.8 million and additional benefits were 1,113 LYs, or 1,117 QALYs, resulting in an incremental cost per LY gained of EUR 18,360 or per QALY gained of EUR 16,750, with vaccination.

Considering a cost-effectiveness threshold of EUR 50,000 per QALY, the net-indirect effects of vaccination need to be at least 16% of those observed in the USA for vaccination to remain cost-effective.

Authors' conclusions
The authors concluded that the cost-effectiveness of routine infant PCV-7 vaccination depended on the inclusion of the indirect effects and these were still uncertain in Europe.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the proposed vaccination strategy was compared against a strategy of no vaccination. The recommended Dutch vaccine dose was used.

Effectiveness/benefits:
The authors provided limited information on the derivation of the clinical inputs and the utility values. A few details on the design of some sources, such as the Dutch studies for the epidemiological data and the clinical trials for the vaccine efficacy, were given, and these appear to have been appropriate. In general, it is difficult to make an objective assessment of the validity of the clinical data given the lack of information. The use of data from multiple sources that might not be comparable, with different patient populations, epidemiological settings, etc., was not investigated. The use of QALYs was valid because the disease has an impact on both survival and quality of life due to the disease sequelae, but no details of the methods used to elicit the utility weights were provided.

Costs:
The economic analysis adopted a broad perspective that included a wide range of items, but the details of the cost categories, unit costs, and data sources were not provided. This limits the transparency of the economic analysis and the possibility of replicating it in other settings. The cost estimates were treated deterministically and the impact of changes in the economic inputs was not investigated.

Analysis and results:
The results were clearly reported and an incremental analysis was appropriately carried out to synthesise the costs and benefits. Conventional Dutch discounting for both the costs and benefits was applied. Conservative assumptions were made when considering the impact of herd immunity. The authors did not perform sensitivity analyses to consider the impact of uncertainty, and focused exclusively on the assumptions on herd immunity, which was consistent with the scope of the study.

Concluding remarks:
The authors' conclusions appear to be valid, but further studies are needed to corroborate the findings, given some limitations in the analysis.
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